# THE INCONSTANCY OF UNIT-CHARACTERS[1]

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THERE can be no reasonable doubt that Mendel's law is of fundamental importance in genetics. It explains so many of the anomalous facts and seeming contradictions encountered in practical breeding. The basic fact underlying this law is the existence of unit-characters, independently inherited. Their independence makes it possible to combine them in any desired way through the agency of cross-breeding.

In the first flush of enthusiasm over the rediscovery of Mendel's law it was thought by some that recombination of unit-characters through crossing was to solve all the problems of breeding relating to the production of new and improved varieties. But experienced animal breeders have, as a rule, been very conservative in their expectations, a conservatism justified by the knowledge of how painfully slow and tedious is the process of improving a breed in any essential regard. For though it is easy enough in two generations to get new color varieties by crossing breeds of different color, the new creations will, in respects other than color, not be the same as either of the breeds crossed; they may be inferior to both in every respect but color, and it will be a difficult, if not impossible, task to restore the desirable qualities lost. The reason is that our improved breeds differ from each other in so many minor characteristics that it is quite impossible to give attention to all of them simultaneously. For as the number of variable characters resulting from a cross increases, a particular combination of characters will become more rare in occurrence and harder to fix.

Soon after it was discovered that unit-characters exist,

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the question was raised whether they are or are not constant.

In our descriptions we call these characters *A, B, C,* etc., and the recombinations are *AB, BC, AC,* etc. In our formulæ *A* is always *A,* and *B* is always *B,* but it is an open question whether in our living animals the characteristics or qualities designated by these symbols are from generation to generation as constant and changeless as the symbols. Bateson and Johannsen and Jennings have assumed that they are, that a horn is always a horn, and a toe a toe. When it is pointed out that horns are not all alike, that they differ in size, shape and color, the reply is made that these differences are due to *other things,* that is, that these are independent qualities not inherent in the horn itself. Now there is force in this argument because we know that a particular color can be dissociated from the horn, why not also size and shape? Nevertheless if we dissociate from the horn *all* color, size and shape we shall have no horn left. The real unit-characters, therefore, which we can think of in a concrete way and deal with in actual breeding operations are differences in *degree* of horn-development, in length, thickness, curvature or coloration. Who shall say whether these differences are few or many? We can conceive of an infinite number of gradations in size, shape and color between known extremes and it is difficult to believe that any one of these is impossible of realization. Nevertheless an important body of present-day naturalists, those who with De Vries believe in mutation, would have us think that these minor gradations are not heritable. Their reasoning is as follows. Suppose we cross horned with hornless cattle. All the immediate offspring are hornless, and the grandchildren 3 hornless to 1 horned. The horned grandchildren breed true. No intermediates occur. Clearly one unit-character difference exists between horns and no horns. Therefore no stable intermediate class can exist unless this unit-character changes. This they consider to be impossible. If we call attention to a *short*-horned race as evidence

that the horn character may vary, they assure us that this condition is due to a different unit and is not derivable from the other, and they challenge us to produce it from the other. If we begin measuring the horns of our cattle and picking out those a little shorter than the average, we find that offspring are obtained with horns of practically average length. Perhaps we repeat the selection half-a-dozen times and begin to get a barely appreciable result. They interrupt, "See here," they say, "you're not getting anywhere; give up and acknowledge yourself beaten. If you stop your selecting for a single generation, the little you have accomplished will disappear. See meantime what we mutationists have accomplished; we have dehorned half-a-dozen breeds by simple crossing. This is more than you could do in a thousand years." Such comment on our work is extremely disquieting, for our progress *is* slow, and we can only reply, "Your method is the quicker one to get rid of a character altogether, but you admit yourself powerless to create a condition which you do not possess fully realized at the outset. We do not admit ourselves so helpless; we hope to get something which we do not now have, and we are willing to wait a while for it. We believe that we can create what does not now exist. This you confess yourself powerless to do."

The foregoing states fairly, I think, the present views regarding selection as a tool of the breeder held on one hand by the mutationists and pure-line advocates, and on the other hand by a minority of Mendelians who like myself consider selection an important creative agency in breeding.

The fundamental point of difference between these two views lies in their different conception of unit-characters. To the mutationist unit-characters are as changeless as atoms and as uniform as the capacity of a quart measure. Theoretically an atom is an atom under all circumstances, and a quart holds the same anywhere and everywhere. But the worldly-wise know that the actual quart is not the same in all places; it is apt to be smaller at the

corner grocery than in the U. S. Bureau of Standards, and the dishonest tradesman will select effectively for diminished size among the various quart measures offered on the market, unless his selection is carefully restrained by legislation. Similarly *actual* unit characters are modifiable under selection; only one blindly devoted to a contrary theory will be able long to shut his eyes to this fact. For several years I have been engaged in attempts to modify unit-characters of various sorts by selection and in every case I have met with success.

I shall speak first of the case least open to objection from the genotype point of view which requires:

1. That no cross breeding shall attend or shortly precede the selection experiment, lest modifying units may unconsciously have been introduced, and

2. That only a single unit-character shall be involved in the experiment.

These requirements are met by a variety of hooded rat which shows a particular black and white coat-pattern. This pattern has been found to behave as a simple Mendelian unit-character alternative to the self condition of all black or of wild gray rats, by the independent investigations of Doncaster and MacCurdy and myself. The pigmentation however in the most carefully selected race fluctuates in extent precisely as it does in Holstein or in Dutch Belted cattle. Selection has now been made by Dr. John C. Phillips and myself through 12 successive generations without a single out-cross. In one series selection has been made for an increase in the extent of the pigmented areas; in the other series the attempt has been made to decrease the pigmented areas. The result is that the average pigmentation in one series has steadily increased, in the other it has steadily decreased. The details of the experiment can not be here presented, but it may be pointed out (1) that with each selection the amount of regression has grown less, *i. e.*, the effects of selection have become more permanent; (2) that advance in the upper limit of variation has been attended by a like recession of the lower limit; the total range of varia-

tion has therefore not been materially affected, but a progressive change has been made in the mode about which variation takes place.

3. The plus and minus series have from time to time been crossed with the same wild race. Each behaves as a simple recessive unit giving a 3:1 ratio among the grandchildren. But the extracted plus and the extracted minus individuals are different; the former are the more extensively pigmented.

4. The series of animals studied is large enough to have significance. It includes more than 10,000 individuals.

The conclusion seems to me unavoidable that in this case selection has modified steadily and permanently a character unmistakably behaving as a simple Mendelian unit.

In my experience *every* unit-character is subject to quantitative variation, that is, its expression in the body varies, and it is clear that these variations have a germinal basis because they are inherited. By selection plus or minus through a series of generations we can intensify or diminish the expression of a character, that is, we can modify the character.

In an earlier lecture I showed that long hair and rough coat in guinea-pigs each differ from the normal condition by a single unit-character. In 1906 I showed that both these characters are subject to quantitative variation, and that such variations are heritable. The same is true of polydactylism in guinea-pigs, a condition in which a fourth toe is present on the hind-foot. A polydactylous race of guinea-pigs was unknown until I created one by selection from among the descendants of a single abnormal individual which had a rudimentary fourth-toe on one hind-foot. For several generations in succession those individuals were selected for parents which had the best-developed extra-toe, and thus was obtained a good 4-toed race.

Another character built up slowly from small beginnings is the silvered variety of guinea-pig. It originated

from a tricolor race in which was observed an individual having white hairs interspersed with red on the lower side of the body. Selection has been made to increase the amount of the silvering and to get it on a black background. This involved increase of the black areas in the coat as also of the silvered areas. In this task, difficult because it involved simultaneous modification of two unrelated characters, steady progress has been made. The best animals are now silvered all over except at the extremities.

Even albinism, the first-discovered of all Mendelian characters in animals and by every one acknowledged to be a single and simple unit-character, even this is variable. In rabbits, for example, some albinos are snow-white without a trace of pigment in the fur or skin, while others (the so-called Himalayan type) are heavily pigmented at the extremities (nose, ears, feet and tail). And yet we can not discover that these two kinds of albinism differ by any second unit-character which might account for the difference. Their albinism is different. Between the extreme types of the snow-white and the Himalayan albino, various intermediates exist, but all are clearly albinos, producing only albinos when bred *inter se*. They represent quantitative variation within the albino type.

Similar quantitative variation within colored classes of animals is well known. Thus in mice an extreme quantitative reduction of the pigmentation has produced an animal with pink eyes and faintly colored coat. Such an animal, however, is not an albino, though less heavily pigmented than many Himalayan rabbits, for if the pink-eyed mouse is crossed with an albino, fully pigmented young result.

In guinea-pigs I several years ago set myself the task of reducing as much as possible the pigmentation of a black race, in hopes thus of obtaining blues. I first crossed the blacks with a light yellow (cream-colored race). In the heterozygotes the black was somewhat reduced in amount. The lightest of these were selected

and again crossed with yellow. By this means the black was after several generations much reduced. The hairs were distinctly yellowish at base and the part above sooty black in appearance. Recently a pink-eyed animal has appeared in this race with hair light sooty-black in spots. This evidently is an extreme variation in the direction which selection has taken throughout the experiment and probably similar in nature to the pink-eyed variation in mice. There can be no question of recombination of independent Mendelian factors in this experiment, because (aside from albinism) only a single Mendelian factor is involved. The heterozygotes, as regards black, have consistently behaved as *simple* heterozygotes, and the experience of all observers agrees with my own that black in guinea-pigs is a simple Mendelian unit. If so it is clearly a unit modifiable under selection.

In yellow animals, as in blacks, individuals of varying intensity occur, the darkest known as reds, the lightest as creams. A complete series of intermediates can be obtained if so desired. If we select any two widely separated stages in this series fairly stable in their breeding capacity and cross these, they Mendelize, *i. e.* they behave as if there were a single unit-character difference between them. Now this fact is instructive, for it throws light on the nature of unit-characters in such cases. They are not things in themselves distinct and separate from the organism concerned; each is a *quantitative variation* plus or minus in some one character possessed by the organism. Each quantitative condition of a character tends to persist from cell-generation to cell-generation. When two quantitatively unlike conditions of a character are brought together in a fertilized egg, they tend to keep their distinctness in subsequent cell-generations and to segregate into different gametes at reproduction, *i. e.,* they Mendelize. Only by a figure of speech are we justified in recognizing a *unit* difference between them. That difference might equally well be *half* as great as it is, or a *quarter* as great, or a thousandth part as great. A mono-hybrid ratio would result

equally in each case, upon crossing the two quantitatively different stages. It is the substantial integrity of a quantitative variation from cell-generation to cell-generation that constitutes the basis of Mendelism. All else is imaginary.

We can distinguish and trace the history of these quantitative variations from generation to generation only when the differences between them are of some size. This has led many to think that only variations of some size are inherited (the mutation theory) and others to deny that such variations can be increased in size by selection (the genotype theory). Others still observing unmistakable evidence that small variations are heritable no less than large ones conceive that the large variations which can be increased or decreased by selection are composed of a certain number of smaller ones cumulative in their effects (the multiple factor hypothesis). A fatal objection to this idea is the fact that these quantitative variations behave as *simple* units, not as multiple ones, and so give mono-hybrid ratios, not polyhybrid ones. The only logical escape from this dilemma for one devoted beyond recall to a pure-line hypothesis will be to assume further that the assumed multiple units are all coupled, *i. e.*, all united in a single material body so that in cell-division they *behave* as one unit, for practical purposes are one unit. This position will be *logically* unassailable, for we shall never know whether the body which in practise behaves as one is in the last analysis composite. Chemists tell us (or used to) that water is composed *ultimately* of atoms of hydrogen and atoms of oxygen not further dissociable, uniform in size and weight and hard and indestructible as rocks; nevertheless for practical purposes we *drink* our cup of water and do not *chew* it. I for one will be content with the admission that variation is as continuous as water and will not press the argument against discontinuity into realms of the ultimate.

The majority of the characters dealt with by the animal breeder are less simple in behavior than color char-

acters. They are also from the economic standpoint more important. Their careful study is therefore desirable. Several years ago I undertook the study of size inheritance in rabbits. I found that when rabbits of unequal size are mated, the young are of intermediate size, *i. e.,* neither large nor small size dominates in the cross. Further, segregation does not apparently occur among the grandchildren, for these vary about the same intermediate mode as the children, though somewhat more extensively. My conclusion was that the inheritance in such cases is non-Mendelian, since neither dominance nor segregation occurs. I called it blending. The experiment with rabbits has been repeated on a much larger scale by my pupil, Mr. E. C. MacDowell. He finds, however, that the variability of the grandchildren is considerably greater than that of the children, though it seldom extends far enough to include the extreme conditions found in the grandparents. This result is confirmed by observations upon ducks made by Dr. Phillips. It is evident therefore that size is not a simple unit-character, for there is no dominance and no evidence of segregation other than the increased variability of the second hybrid generation. But cases of this kind have recently been interpreted as involving multiple unit characters and so as possible Mendelian. This interpretation has been suggested by interesting observations made by Nilsson-Ehle on color-inheritance in oats and wheat.

In crossing colored with uncolored varieties he obtained inheritance ratios of 15:1 or 63:1, instead of the usual 3:1 of colored to uncolored progeny in the second generation from the cross. The ratios obtained in these exceptional cases were such as should occur when two or three independent unit-characters are involved in a cross. But Nilsson-Ehle could discover only a single kind of color-production. The conclusion which one naturally draws from these facts is that the color factor in these cases was localized in two or three distinct bodies independent of each other in their splittings and migrations during cell division. Now Nilsson-Ehle argues with much plaus-

ibility that if in a case such as this dominance were wanting, *i. e.,* if the cross always produced intermediates, the bulk of the second-generation offspring would also be intermediate, with only an occasional complete segregation. He suggests that size differences may involve units of this sort, without dominance though fully segregating. This attractive hypothesis would account for the known facts of size inheritance fairly well, involving only the existence of multiple units which may be perfectly stable and changeless in character. Nevertheless this hypothesis has not been established beyond question. It is quite possible that we are stretching Mendelism too far in making it cover such cases. Dominance is clearly absent and the only fact suggesting segregation is the increased variability of the second as compared with the first hybrid generation. This fact however may be accounted for on other grounds than the existence of multiple units of unvarying power.

If size differences are due to quantitative variations in special materials within the cell, it is not necessary to suppose that these materials are localized in chunks of uniform and unvarying size, or that they occur in any particular number of chunks, yet the genotype hypothesis involves one or both of these assumptions. Both are unnecessary. Variability would result whether the growth-inducing substances were localized or not, provided only they were not homogeneous in distribution throughout the cell. Crossing would increase variability beyond the first generation of offspring because it would increase the heterogeneity of the zygote in special substances (though not its total content of such substances) and this heterogeneity of structure would lead to greater quantitative variation in such materials among the gametes arising from the heterozygote. Thus greater variability would appear in the second hybrid generation.

As a matter of fact we know that protoplasm is not homogeneous, and that there are substances widely distri-

buted in the cell, not localized in chromosomes, which may well have an influence on size.

But whatever our conclusion may be concerning the theoretical explanation of size inheritance, the practical manipulation of it must clearly be different from that of color inheritance. All possible combinations of color factors existing in two distinct races we can secure within two generations by crossing. New conditions of color we can often obtain by the slower process of selection, thus modifying existing color factors. Modification is, I believe, often accelerated by crossing, quite apart from the effect it has in bringing about recombination, because it has a tendency to increase quantitative variation.

Size is an unstable character, ever varying. Slow changes in size can be effected by selection without any crossing whatever. Change in size is made more rapid by crossing, because variability is increased thereby. If further increase in size is desired regardless of other qualities two large races should be crossed and the largest second-generation offspring should be selected. Progressive diminution in size should be sought in a similar way, crossing the smallest breeds.

If a medium-sized race is desired, it may be obtained by crossing a large with a small race and inbreeding the offspring. Physiological limitations undoubtedly would prevent unlimited size variations either plus or minus, yet when we consider what extreme differences exist among dogs, as for example between "toy terriers" and "great Danes," we can scarcely doubt that the limits of possible size variation have not been approached in most of our domesticated animals.